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Epidemiological aspects of opioid use in the metropolitan region of Belo Horizonte, Brazil: the forensic context

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Resumo

Objetiva-se avaliar os óbitos ocorridos em Belo Horizonte e região metropolitana, entre 2006 e 2018, com detecção de opioides nas análises toxicológicas, dado o potencial aumento do uso abusivo destes ao longo dos anos e o impacto social relacionado às vidas perdidas decorrentes de intoxicações. Foi conduzido estudo transversal, retrospectivo, onde foram realizadas medidas de frequência e de tendência central, bem como testes qui-quadrado e teste-t para avaliar independência da distribuição das variáveis, considerando um nível de significância de 95%. Foram analisados 100 laudos de necropsia, onde foi possível perceber aumento da detecção de opioides a partir de 2013. Houve maior prevalência do sexo masculino (65%), sendo a média etária de 48,9 anos. Causa e circunstância de morte indeterminadas foram as mais prevalentes (44%, 61%). Dos óbitos decorrentes de causas externas (33%), quatro decorreram de intoxicação por opioides. A maioria dos periciados recebeu atendimento médico previamente ao óbito (57%). Os opioides tradicionais fortes (82,1%) e naturais (72,6%) foram os mais encontrados, sendo o tramadol o mais observado (35%). A maioria dos casos apresentou alcoolemia negativa (89,6%) e positividade para detecção de psicotrópicos (64%). Os homens apresentam média etária menor, receberam mais atendimento médico e morreram mais por trauma que as mulheres. Apesar de ser considerado um problema de saúde pública importante em outros países, Belo Horizonte e RMBH parece não apresentar, ainda, impacto nas mortes por causas externas. Estudos de maior abrangência devem ser realizados para melhor entendimento em nosso meio.

Palavras-Chave: Opioides, Substâncias Psicoativas, Toxicologia Forense, Medicina Legal.

Abstract

Given the potential increase in the abusive use of opioids over the years and the social impact of lives lost due to poisoning, this study aims to evaluate deaths that occurred in Belo Horizonte and its metropolitan region between 2006 and 2018 with opioid detection in toxicological analyses. A cross-sectional, retrospective study was conducted, in which frequency and central tendency measurements were calculated, and chi-square tests and t-tests were used to assess the independence of variable distributions, considering a significance level of 95%. There was a higher prevalence of males (65%), with an average age of 48.9 years. Undetermined cause and circumstance of death were the most prevalent (44%, 61%, respectively). Of the deaths resulting from external causes (33%), four were due to opioid poisoning. The majority of those examined have received medical care prior to death (57%). Strong traditional opioids (82.1%) and natural opioids (72.6%) were the most frequently found, with tramadol being the most frequently observed (35%). Most cases presented negative blood alcohol levels (89.6%) and positive results for the detection of psychotropic drugs (64%). Men had a lower average age, received more medical care, and died more from trauma than women. Despite being considered an important public health problem in other countries, Belo Horizonte and metropolitan region do not yet appear to have an impact on deaths from external causes. More comprehensive studies must be carried out to better understand our environment.

Keywords: Opioid, Psychoactive Substances, Forensic Toxicology, Forensic Medicine.

1. INTRODUCTION

Opium, extracted from the Papaver somniferum (poppy) plant, has been used for pharmacological purposes since 4,000 BC (1). It contains more than 20 different alkaloids, being recognized for its calming, analgesic and hallucinogenic effects [1].

Opioids (OP) are medications used in cases of moderate to severe pain and are considered highly effective for pain control [1 - 3]. According to 2016 data from the Brazilian Society for Pain Studies (SBED), Brazil is among the ten countries with the lowest rates of opioid prescribing globally, a situation attributed to regulatory mechanisms governing these substances that require special prescription forms [4]. Although this regulation restricts use and abuse of the drug, illegal consumption remains a public health concern [1].

OPs lead to several effects on the body system, such as respiratory, cardiovascular, gastrointestinal and nervous. Overdose can occur accidentally, related drug interactions or intentional abuse [5]. According to the Centers for Disease Control and Prevention, approximately 645,000 individuals died from opioid-related overdoses in the United States between 1999 and 2021 [6]. Among the 200 deaths occurred in Brazil in 2017 related to exogenous poisoning and registered by the National Toxic-Pharmacological Information System, 25% were due medications, but it is not possible to assume how many of these deaths were caused by OP [7].

Among the public policies adopted worldwide in drugs are supply control and free access to social and health services for users, with prevention being the strategy that presents the best cost–benefit ratio for reducing both substance abuse and its consequences [8]. Knowing the situation of substances with potential for abuse and extensive social harm becomes extremely relevant for the formulation of public policies. Considering the potential increase in opioid (OP) abuse over the years and the social impact related to lives lost as a result of poisoning by these medications, this study aims to evaluate deaths that occurred in Belo Horizonte and its metropolitan region between 2006 and 2018 in which OP were detected in toxicological analyses The Legal Medicine Institute André Roquette (Instituto Médico Legal André Roquette - IMLAR) is a public organization related to the State Police, being responsible for the medical investigation of deaths resulting from violent or suspicious causes that occurred in the state capital and in most cities in its Metropolitan Region (RMBH). He is also responsible for the toxicological evaluation of all cases investigated in the state of Minas Gerais. Performing a forensic autopsy for all deaths due to violent causes is mandatory by federal law [9]. Belo Horizonte is the sixth most populous city in Brazil, with 2,521,564 inhabitants and its metropolitan region is the third most populous, with an estimated 5,961,895 inhabitants in 2020 [10].

2. METHODS

A cross-sectional study was carried out with expert reports from IMLAR from 2006 to 2018. Deaths with a positive result (detected) in forensic toxicological tests for one or more OPs whose necropsy reports were available for analysis comprised the study sample. This study included both cases in which death resulted directly from the use of OP and cases in which these were detected but were not associated with the cause of death. The separation of these cases was carried out through a textual search in the Excel® database provided by the Toxicology Laboratory (LABTOX), using the EPI Info7® program.

The information obtained from autopsy procedures and laboratory reports was coded into the following variables:

- Sociodemographic characteristics of the ones inspected: sex, age, skin color;
- General characteristics of the examinations: region of Minas Gerais state from wich the samples originated, year in which the autopsies were carried out, medical care prior to death, circumstances of death (if an accident, suicide or homicide is suspected), medical cause of death;
- Morphological changes observed in the cadavers (on external and internal examination);
- Toxicological tests carried out and their results: type of opioid (potency, origin and function), blood alcohol analysis, other substances of medical interest found.

Not all variables were available for all reports analyzed, including information on the medical history of autopsies.

It was considered that autopsies received medical care before death when they came from health units, when they were sent together with medical reports or when they showed signs of medical procedures such as vascular puncture, recent surgical wounds, among others.

For statistical analysis the IBM SPSS® program, version 20.0, was used. Frequency and central tendency measurements were performed. To test the independence of the distribution of the categorical variables considered, the chi-square test was performed. To test the relationship between a continuous variable and two independent groups, the t-test was performed. For both, a significance levellevel of 95% was considered and their respective confidence interval was presented.

3. RESULTS

An amount of 227 cases with positive toxicological tests for OP were recovered, with their annual distribution shown in Figure 1.

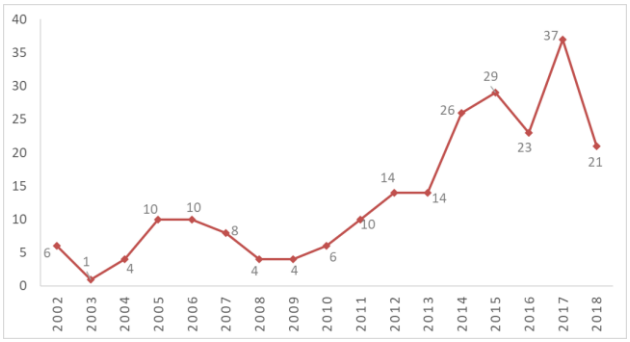

Figure 1. Distribution of positive cases for opioids, by year (IMLAR – 2006 to 2018).

Of the available cases, 100 deaths were analyzed because the respective autopsy reports were recovered. The distribution of these reports, by year, is shown in Figure 2.

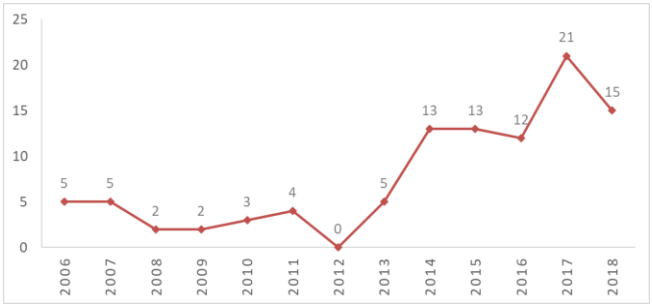

Figure 2. Distribution of autopsies analyzed, by year (IMLAR – 2006 to 2018).

The main victims were male (65% cases), brown (51.5%) and aged ≥ 60 years (32.7%) (table 1). The average age found was 48.9 (SD 25.03) years, with extreme ages ranging from zero to 100 years. The average age of males (44.8) was significantly lower than that of females (56.1) (p=0.032; CI: -21.526 to -0.963). The cases came from the Central region of the State, with only one coming from the Rio Doce region. Medical care was provided to 57% of those examined, proportionally more in men (64.6%) than in women (42.9%) (p= 0.04). There was information on the circumstances of death in 39 cases, of which the suspicion of an accident was the most prevalent (46.2%). The cause of death was undetermined in 44% of cases, external (violent) in 33% and natural (clinical) in 23%. Of the external causes, only four were related to exogenous intoxication (overdose), of which three were associated with psychotropic medications with OP and one with exclusive abuse of OP. There was a significant difference (p=0.026) for the cause of death in relation to gender, with external causes being more prevalent among men (43%) than among women (14.3%) (Table 1).

Table 1. Socio-demographic data of those examined and characteristics of deaths (IMLAR 2006-2018).

		Male		Female		Total	
Color*	**White**	26	40,00%	17	50,00%	43	43,43%
	Brown	35	53,85%	16	47,06%	51	51,52%
	Black	4	6,15%	1	2,94%	5	5,05%
Age Range (years) **	**< 18**	6	9,52%	1	2,86%	7	7,14%
	18 – 29	16	25,40%	5	14,29%	21	21,43%
	30 – 39	6	9,52%	3	8,57%	9	9,18%
	40 – 49	11	17,46%	6	17,14%	17	17,35%
	50 – 59	6	9,52%	6	17,14%	12	12,24%
	60 – 69	6	9,52%	3	8,57%	9	9,18%
	≥70	12	19,05%	11	31,43%	23	23,47%
Medical Care	**No**	23	35,38%	20	57,14%	43	43,00%
	Yes	42	64,62%	15	42,86%	57	57,00%
Cause of death	**Indet.**	23	35,38%	21	60,00%	44	44,00%
	External	28	43,08%	5	14,29%	33	33,00%
	Clinical	14	21,54%	9	25,71%	23	23,00%

Ignored cases = *1 case, **2 cases.
Indet = Indeterminated

Some types of external injuries were observed in 68% of cases. Presence of petechiae was reported in 11% of cases. In most cases, the heart, liver, stomach and brain did not show morphological changes. Brain changes were observed in only 10% of cases, heart hypertrophy/dilation in 29%, liver congestion and/or enlargement in 27%. However, there was foamy secretion in the airways in 53% and the lungs presented foam and/or congestion in 67% (Table 2).

Strong traditional opioids (82.1%) and natural (72.6%) were the most found. Tramadol was detected in 35 cases, codeine in 15, morphine in 13, methadone in 10, fentanyl in 6, and meperidine in 5. For 16 examined individuals, the opioid found was not specified (Untabulated data). Of the 67 cases in which alcohol levels were blood tested,

89.6% presented a negative result, of which 16.7% received hospital care prior to death.

Table 2. Macroscopic necroscopic changes (IMLAR 2006-2018).

		Male		Female		Total	
Presence of external injuries	**No**	18	27,69%	14	40,0%	32	32,0%
	Yes	47	72,31%	21	60,0%	68	68,0%
Presence of foamy secretion in airways	**No**	30	46,15%	17	48,57%	47	47,0%
	Yes	35	53,85%	18	51,43%	53	53,0%
Presence of petechiae	**No**	58	89,23%	31	88,57%	89	89,0%
	Yes	7	10,77%	4	11,43%	11	11,0%
Topography of petechiae	**Head/Neck**	2	3,08%	1	2,86%	3	3,0%
	Chest	6	9,23%	4	11,43%	10	10,0%
	Lungs	2	3,08%	4	11,43%	6	6,0%
	Other (chest)	1	1,54%	0	0%	1	1,0%
Encephalon	**No modification**	54	83,08%	32	91,43%	86	86,0%
	Edema/ Congestion	9	13,85%	1	2,86%	10	10,0%
	Trauma Injury	2	3,08%	1	2,86%	3	3,0%
Heart	**No modification**	40	61,54%	28	80,0%	68	68,0%
	Hypertrophy/ Dilation	22	33,85%	7	20,0%	29	29,0%
	Trauma Injury	3	4,62%	0	0%	3	3,0%
Lung	**No modification**	16	24,62%	15	42,86%	31	31,0%
	Foamy secretion/congestion	47	72,31%	20	57,14%	67	67%
	Trauma Injury	2	3,08%	0	0,00%	2	2%
Liver	**No modification**	41	63,08%	27	77,14%	68	68,0%
	Trauma Injury	5	7,69%	1	2,86%	6	6,0%
	Congestion/Increased	19	29,23%	7	20,0%	26	27,0%

Table 3. Lab tests performed (IMLAR 2006-2018).

		Male		Female		Total	
Alcohol Content	**Unperformed**	19	29,23%	13	37,14%	33	33,00%
	Performed	46	70,77%	22	62,86%	67	67,00%
Alcohol Content results*	**Negative**	42	91,30%	18	85,71%	60	89,55%
	Positive	4	8,70%	3	14,29%	7	10,45%
Presence of opioids and other toxicological drugs	**Yes**	48	73,85%	24	68,57%	72	72,00%
	No	17	26,15%	11	31,43%	28	28,00%
Other substances found in toxicology	**Pesticides**	1	1,54%	0	0%	1	1,00%
	Psychotropics	42	64,62%	22	63%	64	64,00%
	Other drugs	23	35,38%	12	34%	35	35,00%
	Abuse drugs	5	7,69%	2	6%	7	7,00%

Opioid potency**	**Strong**	45	83,33%	24	80,00%	69	82,14%
	Weak	9	16,67%	6	20,00%	15	17,86%
Opioid source	**Natural**	39	72,22%	22	73,33%	61	72,62%
	Synthetic	15	27,78%	8	26,67%	23	27,38%

Ignored data = *1 case, **16 cases (only cited positivity for opioids but did not specify the name of the opioid).

Four of the seven cases with positive alcohol content also received medical care prior to death. The average alcohol content found was 8.8 (SD 8.8) dg/L, extremes of 0.1 and 25.7dg/L. The average blood alcohol level in males was 9.56dg/L and in women it was 7.69dg/L. The toxicological assessment detected pesticides in 1.0% of cases, psychotropic drugs in 64.0%, other medications in 35% and drugs of abuse in 7% (Table 3).

4. DISCUSSION

In the present study, an increase in opioid detection was observed from 2013 onwards. There was a higher prevalence of males, with an average age of 48.9 years. Undetermined cause and circumstance of death were the most prevalent. Of the deaths resulting from external causes, four were due to opioid poisoning. The majority of those examined received medical care prior to death. Strong, natural and traditional opioids were the most found, with tramadol being the most observed. Blood alcohol level was negative for the majority, as well as detection of psychotropic drugs. Men have a lower average age, received more medical care and died more from trauma than women. Most of those examined presented some type of external injury and foamy secretion in the airways and lungs upon necroscopic examination.

Over the last few years there has been a worldwide increase in OP prescriptions for the treatment of chronic non-cancer pain (76% between 2010 and 2019), also increasing abuse and overdose mortality related to these substances [11,12]. In 2019, 10 million Americans reported some use of OP outside of the hospital setting. Between 2010 and 2019 the number of users on the African and Asian continents doubled from 31 to 62 million. In South America, there were 600 thousand users in Chile (2018), Uruguay (2018) and Colombia (2019) [11]. The estimated use (medical and/or abusive) of OP in South America is just 0.2%, without alarming numbers of overdose deaths compared to data from North America, where numbers doubled between 2010 and 2019 (from 21 to 50 thousand deaths). The high general consumption of OP increases its illegal trade. Although this is not very common in Brazil, it is significant in the USA, Canada, and Mexico. The latter is the main place where the plant grows in Latin America. This corroborates the data from the present study, in which the detection of OP use was low, as was the number of deaths related to its abuse. Although the Brazilian numbers are not so alarming, especially because of regulatory prescription measures, and given the proportions in the rest of the world, it is important to monitor occurrences, such as the data presented here. Transformations in use/abuse are direct consequences of globalization.

The increase in OP-positive cases in IMLAR toxicological tests from 2013 onwards in this study may be related to greater ease of access to autopsy reports during this period. There was a change in the platform for preparing and storing reports by the Civil Police of Minas Gerais beginning in 2012, when the process became digital through the PCNet system (Sistema de Informatização e Gerenciamento dos Atos de Polícia Judiciária - Police Information and Case Management System). According to the mortality information system (SIM - Sistema de Informações sobre Mortalidade), between 2006 and 2018, 95 drug-related deaths were reported in the metropolitan region of Belo Horizonte (RMBH), and it is not possible to discriminate how many were related to the use of OP. OP poisoning was the cause of death in only four of the 33 deaths from external causes observed in the present study, and was therefore not an important death condition in RMBH.

These results are consistent with those observed in a study conducted in ten Brazilian capitals, which highlighted the low consumption of these substances, with OP dependence being more prevalent among healthcare workers (13). As opioids are medications dispensed only upon presentation of a prescription and are subject to strict regulation by ANVISA, access among healthcare professionals—particularly physicians—appears to be higher than in the general population [13].

It is noteworthy that there are no macroscopic or microscopic necroscopic findings specific to a death resulting from OP poisoning. This diagnosis is given through the history of the occurrence (when available), the necroscopic exclusion of other causes of death in the case analyzed and the performance of toxicological analyzes with the detection of any OP [14]. Therefore, it is possible that in some cases, even if the death resulted from the use of OP, it was not possible to establish this connection, due to the lack of reliable information about what happened, the time elapsed between use and death, due to a possible medical care provided or even due to

some other factor that may have influenced the necroscopic findings and toxicological analyses, such as putrefaction, for example.

OPs were most detected in deaths from natural causes (23 cases) in IMLAR, as they are used to treat pain in several chronic conditions, especially those of oncological origin, as well as for medical procedures such as orotracheal intubation [15]. These are medications prescribed to treat pain, according to the intensity scale proposed by the WHO (World Health Organization) and are indicated for 2nd and 3rd degree pain. However, the management of pain symptoms can become inadequate and ineffective owing to barriers related to availability and accessibility. Narcotic medications present on ANVISA (Brazilian National Health Surveillance Agency) control lists A1 and A2 require notification and retention of "A" (yellow) prescription. Included in the substances present in these lists are OPs such as oxycodone (above 40 mg per dosage unit - A1), and acetyl dihydrocodeine, codeine, dihydrocodeine, ethylmorphine, pholcodine, nicodicodine and norcodeine (all above 100 mg per dosage unit and with concentrations greater than 2.5% in preparations - A2) [16, 17]. As a result of such legal obligations, there may be low prescription of these, also reflecting their lower demand for recreational purposes (abuse) [15, 18]. It is understood that there is a direct relationship between the frequency of OP prescription and its abusive use, with greater susceptibility to addiction occurring among people who are treated with such medications. Because of the possibility of dependence, numerous factors must be considered before prescribing them, including some that indicate greater caution: young people, chronic pain after car accidents, previous or current use of illicit drugs, depression and use of psychotropic medications, smoking, alcoholism, among others [19].

The use of OP related to clinical conditions (natural) in autopsies in this study is probably greater since there was no significant difference between deaths of undetermined cause and those of clinical cause. The undetermined deaths in this sample (44 cases) are, presumably, natural, which adds up to 77% of deaths from non-external causes related to the use of OP. It should be noted that it is not the role of Forensic Medicine to investigate deaths from natural causes. The basic indication of medical legal necropsy is the medical investigation of violent deaths, which is mandatory under article 158 of the Brazilian Code of Criminal Procedure (9). Natural deaths without medical assistance should be analyzed by the Death Verification Service, unfortunately not yet available in Belo Horizonte [20]. An important mechanism of death in many natural deaths involves failure of the heart as a pump, producing cardiogenic pulmonary edema and increased secretion in the airways, explaining the necroscopic findings in our sample [5]. OPs are also indicated in the treatment of some types of trauma, which justifies their presence in at least part of the 33 cases related to trauma deaths. It also should be noted that the use of OP is more restricted in emergency care as its side effects can produce complications in this situation, and is generally prescribed by pain specialists, neurologists, anesthesiologists, orthopedists and geriatricians, different situations other than the trauma ones [21].

The sample of the present study was mainly composed of adults and elderly people, more prone to chronic diseases, with natural causes deaths predominantly, which may justify the number of cases receiving medical care prior to death, with an associated prescription of OP. Tramadol was the most commonly found OP, being indicated for the treatment of moderate to severe pain (2nd grade on the WHO scale). Its prescription is justified in cases of hospitalization due to clinical and/or surgical diseases, as well as in elderly people (aged 60 years or over), a large part of the present sample.

Most of male individuals observed in the present study had external causes of mortality. According to the Profile of the Situation of Men's Health in Brazil from the Ministry of Health (2012), the mortality rate among men is 2.3 times higher than among women, and they are more likely to be involved in accidents and other situations. forms of violence [22]. The propensity for violent deaths among young males is greater in Latin American countries; In Brazil, violence is the main cause of death among young men [11]. For every 1% increase in the proportion of the population aged between 15 and 29 years, there is a potential 2% increase in the homicide rate [23]. Male individuals are also more predisposed to death caused by OP abuse in self-extermination, although deaths caused by exogenous intoxication by this substance, in males, were only two of the four cases in IMLAR [23]).

Most autopsies (89.5%) did not show positive blood alcohol levels, which can be explained by the fact that there was a history of hospital care prior to death in most cases. The concomitant use of OP and alcohol is also not common in our country, as both are depressants of the central nervous system and OPs decrease activity and promote less absorption of alcohol in the body due to reduced gastric emptying rate [24].

Furthermore, in 72% of cases evaluated in IMLAR, other medications were detected in toxicological tests, especially psychotropic drugs. The fact that the sample is made up of adults and the elderly, who are more likely to have chronic diseases, such as cancer, may justify the use of more than one medication; among the elderly, polypharmacy is quite common [25].

Another important aspect to consider is that this study covered until 2018, therefore prior to the COVID-19 pandemic. There is evidence, at least in the United States,

that the period of social isolation imposed by the pandemic contributed to the increase in the number of deaths resulting from the use/abuse of OP [26]. An American study with data from 49 states indicated a 42.1% increase in cardiac arrests resulting from exogenous poisoning (overdose) in 2020 [27]. Therefore, new studies must be carried out to verify whether the pandemic has changed the profile of use and deaths from OP in our country.

The following stand out as biases in this study:

- The number of reports with OP detection analyzed (100) and the fact that almost all of them came from a specific geographic region (BH and RMBH);

- Difficulties in obtaining autopsy reports for all deaths evaluated, especially for cases evaluated in the interior of the state of Minas Gerais;

- All information was obtained from reading necroscopic and toxicological reports (secondary sources), prepared by different medical examiners and toxicologists, corroborating the heterogeneity in the performance of each exam, including influencing which complementary exams were requested in each of the reports.

5. CONCLUSIONS

IMLAR data indicate that the detection of OP in post-mortem toxicological tests was more often related to their use in treating natural diseases than to poisoning from their abuse. Traditional, strong and natural OPs agonists were the most found. Despite being considered an important public health problem in other countries, particularly in the United States, the use of OP in Belo Horizonte and RMBH does not yet seem to have an impact on deaths from external causes. However, larger studies, with more data from MG and other states, must be carried out to better understand OP-related deaths in our country.

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